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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,377	02/26/2002	Catherine Defrenne	GSKB-109US	4141

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EXAMINER	
BASKAR, PADMAVATHI	
ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/936,377	DEFRENNE ET AL.	
	Examiner	Art Unit	
	Padma V. Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,29,31,32,35,40,41,43,50,51,57 and 59-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *25,32,35,40,41,43,60,64 and 67* is/are allowed.

6)☒ Claim(s) *29,31,50,51,57,59,62,63,65,66 and 68-72* is/are rejected.

7)☒ Claim(s) *61* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/28/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants submission filed on 8/28/08 has been entered. MPEP 7.42.04.

Amendment

2. The amendment filed on 8/28/08 is acknowledged and entered.

Status of claims

3. Claims 25, 29, 31-32, 35, 40-41, 43, 50-51, 57, and 59-72 are pending.
Claims 27, 48, and 49 are canceled .
Claims 25, 29, 31, 35, 40, 50, and 57 have been amended.
New claims 64-72 have been added.

Information Disclosure Statement

4. The Information Disclosure Statement filed on 8/28/08 has been reviewed and a signed copy of the same is attached to this action.

Claim objection

5. Claim 61 is objected as it depends on a canceled claim 48.

Claim Rejections - 35 USC 112, first paragraph

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 29, 31, 50-51, 57, 59, 62-63 , 65-66 and 68-72 are rejected under 35 U.5.C. 112, first paragraph , as containing subject matter which was not described in the specification

in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical characteristics and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (see MPEP 2163).

The claims are drawn to an isolated polypeptide comprising an immunogenic fragment of at least 15 or 20 contiguous amino acids of SEQ ID NO:2, wherein the immunogenic fragment when administered to a subject as a conjugate with a suitable carrier or in a composition which can include an adjuvant, is capable of inducing an antibody that specifically binds to said fragment within SEQ ID NO:2 . Claims are also drawn to fusion protein and immunogenic composition comprising said fragments. Thus, the scope of the claims includes a genus of polypeptides and the genus is highly variant, inclusive to numerous structural variants because a significant number of structural differences between genus members is permitted. The specification teaches a single isolated polypeptide SEQ ID NO: 2 comprising the 758 amino acid sequence set forth as SEQ.ID.NO: 2 from *Neisseria meningitidis* serogroup *B* strain ATCC 13090 which is designated as a " BASB082" polypeptide in example 2 (page 69) . The specification does not place any structure, chemical or functional limitations on the fragments embraced by "15 or 20 contiguous amino acids of SEQ.ID.NO: 2". The recitation of "15 or 20 contiguous amino acids of SEQ.ID.NO: 2 does not convey a common structure or function and is not so defined in the specification. Although the specification teaches that variants can be readily screened, the specification and the claim do not provide any guidance on the structure of the polypeptide and what changes can or can not be made. For example, Lederman et al (Molecular Immunology 28:1171-1181, 1991) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document). Li et al (Proc. Natl. Acad. Sci. USA 77:3211-3214, 1980) disclose that dissociation of immunoreactivity from other activities when constructing analogs (see entire document). "A patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed

a single species when … the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed." *In re Curtis*, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004). For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. See, e.g., *Eli Lilly*.

Further, it is not sufficient to define it solely by its principal biological property, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. Per the *Enzo* court's example, (*Enzo Biochem, Inc. v. Gen-Probe Inc*., 63 USPQ2d 1609 (CA FC 2002) at 1616) of a description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) couched "in terms of its function of lessening inflammation of tissues" which, the court stated, "fails to distinguish any steroid from others having the same activity or function" and the expression "an antibiotic penicillin" fails to distinguish a particular penicillin molecule from others possessing the same activity and which therefore, fails to satisfy the written description requirement. Similarly, the function of binding to the claimed antibodies does not distinguish a particular "15 or 20 contiguous amino acids of SEQ.ID.NO: 2" polypeptide from others having the same activity or function and as such, fails to satisfy the written-description requirement. Applicant has not disclosed any relevant, identifying characteristics, such as structure or other physical and/or chemical properties, sufficient to show possession of the claimed genus. Mere idea or function is insufficient for written description; isolation and characterization at a minimum are required. A description of what a material does, rather than what it is, usually does not suffice. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

Structural features that could distinguish a "15 or 20 contiguous amino acids of SEQ.ID.NO: 2" polypeptide in the genus from others in the protein class are missing from the disclosure and the claims. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description, because specific, not general guidance is needed. Since the disclosure does not describe the common attributes or structural characteristics that identify members of the genus, and because the genus is highly variant, the function of the binding of antibody alone is insufficient to describe the genus of "15 or 20 contiguous amino acids of SEQ.ID.NO: 2" polypeptides of that function equivalently. One of skill in the art would reasonable conclude that the disclosure of a single polypeptide, i.e., SEQ ID NO:2, does not provide a representative number of species of SEQ.ID.NO: 2 to describe the claimed genus and as a consequence antibodies that bind such.

The recitation of "15 or 20 contiguous amino acids of SEQ.ID.NO: 2" does not convey a common structure nor a common function. As such, generic polypeptide sequences that are unrelated via structure and function are highly variant and not conveyed by way of written description by the specification at the time of filing. As such the specification lacks written description for the highly variant genus of single function polypeptides (antibody binding) and one skilled in the art would not recognize that applicants had possession of the genus of claimed polypeptides for antibody binding as instantly claimed.

Therefore, only the polypeptide set forth as SEQ ID NO:2, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

8. Claims 29, 31, 50-51, 57, 59, 62-63 , 65-66 and 68-72 are rejected under 35 U.S.C. 112, first paragraph while being enabling for an isolated polypeptide comprising the amino acid sequence SEQ ID NO: 2, fusion protein comprising the amino acid sequence of SEQ ID NO: 2 and an immunogenic composition comprising the amino acids sequence SEQ ID NO: 2 does not reasonably provide enablement an isolated polypeptide comprising an immunogenic fragment of at least 15 or 20 amino acids of SEQ.ID.NO: 2, fusion protein comprising said fragments and immunogenic composition comprising said fragments. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir.1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the predictability or unpredictability of the art, (5) the relative skill of those in the art, (6) the amount or direction or

guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary. Although the quantity of experimentation alone is not dispositive in a determination of whether the required experimentation is undue, this factor does play a central role. For example, a very limited quantity of experimentation may be undue in a fledgling art that is unpredictable where no guidance or working examples are provided in the specification and prior art, whereas the same amount of experimentation may not be undue when viewed in light of some guidance or a working example or the experimentation required is in a predictable established art. Conversely, a large quantity of experimentation would require a correspondingly greater quantum of guidance, predictability and skill in the art to overcome classification as undue experimentation. In Wands, the determination that undue experimentation was not required to make the claimed invention was based primarily on the nature of the art, and the probability that the required experimentation would result in successfully obtaining the claimed invention. (Wands, 8 USPQ2d 1406). Thus, a combination of factors which, when viewed together, would provide an artisan of ordinary skill in the art with an expectation of successfully obtaining the claimed invention with additional experimentation would preclude the classification of that experimentation as undue. A combination of Wands factors, which provide a very low likelihood of successfully obtaining the claimed invention with additional experimentation, however, would render the additional experimentation undue.

1-2 Breadth of the claims and the nature of the invention: In regards to recombinant isolated polypeptide SEQ.ID.NO:2 of the invention and the breadth of the claims , the broadest interpretation that applies is fragments of SEQ.ID.NO:2

3-4 The state of prior art and the level of predictability in the art: The state of the prior art with respect to fragments, Herbert et al (The Dictionary of Immunology, Academic Press, 3rd Edition, London, 1985, pages 58-59). specifically teach that an epitope is the region on an antigen molecule to which antibody specifically binds. B cell epitopes on protein antigens are of variable size comprising up to about 20 amino acids. Antibodies bind in a more or less exact three dimensional fit with an epitope. This may be formed from residues on different regions of a protein antigen molecule which, in the native state, are closely apposed due to protein folding. Thus the three-dimensional structure of the protein molecule may be essential for antibody binding. (p. 58). Lederman et al (Molecular Immunology 28:1171-1181, 1991) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document). Li et al (Proc. Natl. Acad. Sci. USA 77:3211-3214, 1980) disclose that

dissociation of immunoreactivity from other activities when constructing analogs (see entire document).

5. The relative skill in the art: The relative skill in the art as it relates to the fragments of the invention is characterized by that of a M.D. or Ph. D. level individual.

6-7. The amount of guidance present and the existence of working examples: The specification teaches a single isolated polypeptide SEQ ID NO: 2 comprising the 758 amino acid sequence set forth as SEQ.ID.NO: 2 from *Neisseria meningitidis* serogroup *B* strain ATCC 13090 which is designated as a "BASB082" polypeptide.

The specification provides no guidance or working examples which would provide guidance to one skilled in the art as to which amino acids or polypeptide fragments are critical to the production of antibodies which recognize said fragment full length SEQ ID NO:2 and no evidence has been provided which would allow one of skill in the art to predict which of the broadly claimed polypeptide fragments would function as claimed with a reasonable expectation of success

8. The quantity of experimentation necessary: The amount of experimentation that is required is undue. While preparing recombinant polypeptide is routine, an immunogenic fragment of at least 15 or 20 contiguous amino acids of SEQ ID NO:2, wherein the immunogenic fragment when administered to a subject as a conjugate with a suitable carrier or in a composition which can include an adjuvant, is capable of inducing an antibody that specifically binds to said fragment within SEQ ID NO:2 is not routine and requires more experimentation because which amino acid residues in SEQ.ID.NO:2 are critical for inducing an antibody that specifically binds to fragment within SEQ ID NO:2 is not set forth .Therefore, in view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, and the high degree of unpredictability as evidenced by the prior art, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention.

It must be noted that the issue in this case is the breath of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record. The Applicants make and test position is inconsistent with the decisions of *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) where it is stated that "... scope of claims must bear a

reasonable correlation to scope of enablement provided by the specification to persons of ordinary skill in the art...". Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands*, 858 F.2d at 737, 8 USPQZd at 1404 (Fed. Cir. 1988). Therefore, for the instant specification to be enabling, it needs to provide direction/guidance regarding an acceptable number of different variants/fragments of SEQ ID NO:2.

Absent sufficient guidance/direction one of skill in the art would not be able to practice the claimed invention commensurate in scope with the claims. Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention as the amount of experimentation required is undue, due to the broad scope of the claims, the lack of guidance and insufficient working examples provided in the specification and the high degree of unpredictability as evidenced by the state of the prior art, attempting to test all the different type fragments of SEQ ID NO:2 encompassed by the claimed invention would constitute undue experimentation. Therefore, applicants have not provided sufficient guidance to enable one of skill in the art to make and use the claimed invention in a manner that reasonably correlates with the scope of the claims, to be considered enabling.

Conclusion

9. Claims 25, 32, 35, 40-41, 43, 60, 64 and 67 are allowable.
Claim 61 is objected as it depends on a canceled claim 48.
Claims 29, 31, 50-51, 57, 59, 62-63 , 65-66 and 68-72 are rejected.

10. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published in the Official Gazette, 1096 OG 30, November 156, 1989. The Right Fax number is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PMR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PMR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571) 272-0956.

Respectfully,

/Padma V Baskar/

Examiner, Art Unit 1645

/Robert B Mondesi/

Supervisory Patent Examiner, Art Unit 1645